comprising a heterologous G protein-coupled receptor, and a mutation of a host cell gene that results in an improved functional response of the G protein coupled receptor in a cell-based assay to a test compound; and (b) measuring the effect of the test compound on cell growth.

Please cancel claims 1, 27, 30-31, 36-37, and 42-51 without prejudice or disclaimer of the subject matter recited therein and enter new claims 52-85:

--52. (New) The method of claim 26, wherein the mutation results in improved agonist stimulated growth promoting ability.

53. (New) The method of claim 26, wherein the host cell gene encodes a regulatory receptor protein kinase, and the mutation causes a reduction in receptor phosphorylation.

54. (New) The method of claim 53, wherein the regulatory receptor protein kinase is selected from the group consisting of G protein-coupled receptor kinases, protein kinase A, protein kinase C and casein kinase.

55. (New) The method of claim 26, wherein the host cell gene encodes a component of the endocytic or degradative pathway and the mutation causes a reduction in receptor sequestration, internalization, or degradation.

56. (New) The method of claim 26, wherein the mutation affects the ratio or nature of sterols in the host cell membrane.

57. (New) The method of claim 56, wherein the host cell gene is selected from the group consisting of *ERG2*, *ERG3*, *ERG4*, *ERG5*, and *ERG6*.

58. (New) The method of claim 57, wherein the host cell gene is *ERG6* and the heterologous G protein-coupled receptor is selected from the group consisting of a

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human melanocortin receptor, a rat somotostatin SSTR2 receptor, a rat M3 muscarinic acetylcholine receptor, and a rat CCKB receptor.

59. (New) The method of claim 56, wherein the host cell gene is selected from the group consisting of *HEM1*, *HEM3*, *SUT1*, *PDX3*, *UPC1*, and *UPC2* (*UPC20*) and wherein the mutation allows the host cell to grow in the presence of exogenously added sterols.

60. (New) The method of claim 13, wherein the heterologous G protein-coupled receptor is modified at an intracellular domain of the G protein-coupled receptor.

61. (New) The method of claim 13, wherein the intracellular domain is the third intracellular loop.

B3

62. (New) The method of claim 13, wherein the heterologous G protein-coupled receptor is an orphan receptor.

63. (New) The method of claim 61, wherein the heterologous G protein-coupled receptor is an orphan receptor.

64. (New) The method of claim 13, wherein the heterologous G protein-coupled receptor is modified at amino acid residues Asp-Arg-Tyr in the domain proximal to the second intracellular loop of the G protein-coupled receptor.

65. (New) The method of claim 60, wherein the modified G protein-coupled receptor is a human alpha 2A adrenergic receptor and the modification comprises a point mutation of threonine to lysine at amino acid residue 373.

66. (New) The method of claim 65, wherein the modification further comprises a truncated third intracellular loop having 44 amino acids.

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67. (New) The method of claim 64, wherein the heterologous G protein-coupled receptor is a M3 muscarinic acetylcholine receptor.

68. (New) The method of claim 67, wherein the aspartic acid residue is replaced by a hydrophobic amino acid.

69. (New) The method of claim 68, wherein the hydrophobic amino acid is isoleucine.

70. (New) The method of claim 13 or 26, wherein the host cell comprises a modified G protein alpha subunit gene that encodes a chimeric G alpha protein.

71. (New) The method of claim 70, wherein the modified G protein alpha subunit gene comprises a first nucleic acid sequence encoding the amino terminal domain of an endogenous G alpha protein, linked to a second nucleic acid sequence encoding the carboxy terminus of a heterologous G alpha protein.

B3

72. (New) The method of claim 70, wherein the modified G protein alpha subunit gene comprises a substitution of a first nucleic acid sequence encoding the five carboxy terminal amino acids of an endogenous G alpha protein for a second nucleic acid sequence encoding the five carboxy terminal amino acid sequences of a heterologous G alpha protein.

73. (New) The method of claim 71, wherein the amino terminal domain of the G alpha protein comprises an interaction domain for a G beta protein, a G gamma protein, and an effector molecule.

74. (New) The method of claim 71 or 72, wherein the modified G protein alpha subunit gene is *GPA1*.

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75. (New) The method of claim 71 or 72, further comprising a heterologous G protein-coupled receptor.

76. (New) The method of claim 75, wherein the modified G protein alpha subunit gene is *GPA1*.

77. (New) The method of claim 75, wherein the heterologous G alpha protein is a mammalian protein.

78. (New) The method of claim 76, wherein the modified *GPA1* gene comprises a first nucleic acid sequence encoding the amino terminal domain of an endogenous G alpha protein, linked to a second nucleic acid sequence encoding the carboxy terminus of a mammalian G alpha protein selected from the group consisting of Gαi2, Gαi3, Gαo, Gαs, Gαq, Gαz, Gα11, Gα12, Gα13, Gα14, Gα15, and Gα16.

B3

79. (New) The method of claim 76, wherein the modified *GPA1* gene comprises a substitution of a first nucleic acid sequence encoding the five carboxy terminal amino acids of an endogenous G alpha protein for a second nucleic acid sequence encoding the five carboxy terminal amino acid sequences of a mammalian G alpha protein selected from the group consisting of Gαi2, Gαi3, Gαo, Gαs, Gαq, Gα11, Gαz, Gα12, Gα13, Gα14, and Gα15, and Gα16.

80. (New) The method of claim 77, wherein the heterologous G protein-coupled receptor is selected from the group consisting of rat somatostatin SSTR2, rat adenosine A2a, rat muscarinic acetylcholine M2 and M3, *D. melanogaster* muscarinic acetylcholine M1, rat neurotensin NT-1, human vasopressin V2, rat cholecystokinin CCK-A and CCK-B, human gonadotropin releasing hormone GnRH, human melanocortin MCR4, human

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adrenergic α2A, *Aplysia californica* octopamine OA1, human bombesin receptor related sequence 3 (BRS3), human histamine H3, and human β2-adrenergic receptor.

81. (New) A method for screening compounds capable of binding to G protein-coupled receptors, said method comprising:

(a) expressing constitutively active heterologous G protein-coupled receptors in a yeast host cell comprising:

(i) transforming the host cell with a vector comprising a DNA sequence encoding a modified heterologous G protein-coupled receptor, wherein the modification results in a constitutively active G protein-coupled receptor; and

B3

(ii) culturing the transformed host cell to permit expression of the heterologous G protein-coupled receptor.

(b) subjecting a yeast host cell comprising a heterologous G protein-coupled receptor, and a mutation of a host cell gene that results in an improved functional response of the G protein coupled receptor in a cell-based assay to a test compound; and

(c) measuring the effect of the test compound on cell growth.

82. (New) The method of claim 13 or 26, further comprising measuring agonist-stimulated activation of a heterologous G protein-coupled receptor in a host cell comprising:

(a) transforming a host cell comprising a modified G protein alpha subunit gene which encodes a chimeric G alpha protein with a vector comprising a DNA sequence encoding a heterologous G protein-coupled receptor;

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(b) culturing the transformed host cell in the presence of an agonist specific for the heterologous G protein-coupled receptor; and

(c) measuring the growth of the host cell in response to the agonist to determine the agonist-stimulated activation of the heterologous G protein-coupled receptor.

83. (New) The method of claim 13 or 26, further comprising measuring the coupling specificity of a G alpha protein for a heterologous G protein-coupled receptor comprising:

(a) transforming a yeast host cell comprising a modified G protein alpha subunit gene which encodes a chimeric G alpha protein with a vector comprising a DNA sequence encoding a heterologous G protein-coupled receptor;

133

(b) culturing the transformed host cell in the presence of an agonist specific for the heterologous G protein-coupled receptor; and

(c) measuring the growth of the host cell in response to the agonist to determine the coupling specificity of the G alpha protein for the heterologous G protein-coupled receptor.

84. (New) The method of claim 13 or 26, further comprising measuring agonist-stimulated activation of a heterologous G protein-coupled receptor in a host cell comprising:

(a) culturing a yeast host cell in the presence of an agonist specific for the heterologous G protein-coupled receptor; and

(b) measuring the growth of the host cell in response to the agonist to determine the agonist-stimulated activation of the heterologous G protein-coupled receptor.

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